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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/713,424 | 11/17/2003 | Gai Ling Li | 6102-000071/US | 4527 |

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| EXAMINER | |
|---|---|
| CLAYTOR, DEIRDRE RENEE | |
| ART UNIT | PAPER NUMBER |
| 1617 | |
| MAIL DATE | DELIVERY MODE |
| 06/25/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/713,424 | LI ET AL. | |
| | Examiner | Art Unit | |
| | Renee Claytor | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2-7,9 and 16-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7, 9, 16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/14/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

Applicants arguments filed on 3/14/2008 have been fully considered. In particular Applicants arguments over the 35 USC 103 rejection over Muller in view of Panchagula and Suzuki have been fully considered. In particular, Applicants argue that Muller teaches the release of the free base of rotigotine as being markedly improved over the use of salts and therefore teaches away from using salts. Applicants further argue that Panchagula merely summarizes the hope and potential surrounding iontophoresis and remarks on limitations and practical considerations concerning iontophoresis. It is further argued that Suzuki does not provide information on the concentration of the salts used and does not indicate a preference for the chloride salt as compared to the other salts listed.

In response to the above arguments, it is noted that Muller teaches that the solubility of the free base of rotigotine is more soluble than the hydrochloride salt so that the active substance is preferably only partially dissolved. It is further taught that the hydrochloride salt passes the stratum corneum poorly and it necessary to use the lipophile and monovalent acids to convert the hydrochloride into the more lipophilic oleate and acts as a permeation enhancer in the skin. Therefore, although it is taught that in the invention of Muller the free base is more soluble, it is further taught to use lipophiles and monovalent acids in an effort to enhance penetration into the skin which reads on the present claims as written which comprises rotigotine and a chloride salt.

In response to the arguments over Panchagula are not persuasive because Panchagula is used to show that this is a method of transdermally delivering

compounds across the skin. Panchagula also discusses methods of using iontophoresis, such as electro-osmosis, that is important with large ions. As with any system of drug delivery, limitations are recognized. However, Panchagula teaches various systems of iontophoretic devices that deliver various types of compounds. Regarding the choice of salts used, it is noted that chlorides provide a positive and negative charge to aid in transporting compounds through the skin. By applicant's own admission in the specification in the last paragraph on page 7 spanning into page 8, all chloride salts which are pharmaceutically acceptable may be employed in the composition of the invention. It is also taught that NaCl, triethylammonium chloride and tributylammonium chloride are art equivalent as being used in the invention. Accordingly, it would be obvious to use any chloride salt in the invention to aid in the transdermal delivery of rotigotine.

Accordingly, the following modified rejection is given below.

***Claim Rejections – 35 U.S.C. § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-7 and 9, 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muller et al. (US Patent 6,884,434) in view of Panchagnula et al. (Curr Op Chem Biol 2000, 4:468-473) and Suzuki et al. (US Patent 6,416,503).

Muller et al. teach a transdermal therapeutic system comprised of rotigotine in the hydrochloride form (see Col. 1, lines 9-25 and Examples 3-7). It is further taught that this transdermal therapeutic system is used for the treatment of Parkinson's disease (Col. 1, lines 9-10).

Muller et al. does not teach treating Parkinson's disease transdermally by application of an iontophoretic device, the concentration of rotigotine, the concentration of the chloride salt with a pH of 4 to 6.5 or the specific chloride salts as claimed in claims 4 and 5.

Panchagnula et al. teaches that iontophoretic transport involves movement of molecules across the skin (see second and third paragraph in column 2, page 468). Table 1 shows iontophoretic products under development, one of which includes a wearable iontophoretic patch (page 469). In addition it is further taught that a hydratable gel pad is also useful (last paragraph page 470).

Suzuki et al. teach iontophoretic drug devices that contain sodium chloride (Col. 7, lines 1-3).

Furthermore, it is obvious to vary and/or optimize the amount of rotigotine, amount of chloride salt and pH provided in the composition, according to the guidance provided by Muller et al. and Suzuki et al. to provide a composition having the desired properties such as the desired concentrations of rotigotine, chloride salt and pH in order to effectively construct an iontophoretic device that will effectively transfer drug through the skin. It is noted that "[W]here the general conditions of a claim are disclosed in the

prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Muller et al., which teach a method of treating Parkinson's disease with a transdermal patch containing rotigotine hydrochloride, with the teachings of Panchagnula et al., which teach transdermal delivery of drugs via iontophoresis, including a patch and Suzuki et al. which teach the use of sodium chloride in an iontophoretic device. Due to Applicants own admission in the specification spanning the last paragraph of page 7 to page 8, any pharmaceutically acceptable chloride salt can be used in the invention and teaches equivalency of NaCl, triethylammonium chloride and tributylammonium chloride which would lead one of ordinary skill in the art to believe that any of the 3 above mentioned chloride salts are equivalent and can be used in the invention. One would have been motivated to use iontophoresis as a method to transdermally deliver rotigotine hydrochloride because it is an efficient method to deliver drugs and cost effective (as taught by Panchagnula et al.) and to add sodium chloride in an effort to further improve drug delivery (as taught by Suzuki et al.).

***Conclusion***

No claims are allowed.

***Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617